

Research Paper

Renal Transplantation: Relationship between Hospital/Surgeon Volume and Postoperative Severe Sepsis/Graft-Failure. A Nationwide Population-Based Study

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Abstract

Background and objects: We explored the relationship between hospital/surgeon volume and postoperative severe sepsis/graft-failure (including death).

Methods: The Taiwan National Health Insurance Research Database claims data for all patients with end-stage renal disease patients who underwent kidney transplantation between January 1, 1999, and December 31, 2007, were reviewed. Surgeons and hospitals were categorized into two groups based on their patient volume. The two primary outcomes were severe sepsis and graft failure (including death). The logistical regressions were done to compute the Odds ratios (OR) of outcomes after adjusting for possible confounding factors. Kaplan-Meier analysis was used to calculate the cumulative survival rates of graft failure after kidney transplantation during follow-up (1999-2008).

Results: The risk of developing severe sepsis in a hospital in which surgeons do little renal transplantation was significant (odds ratio [OR]; $p = 0.0115$): 1.65 times (95% CI: 1.12-2.42) higher than for a hospital in which surgeons do many. The same trend was true for hospitals with a low volume of renal transplantations (OR = 2.39; 95% CI: 1.62-3.52; $p < 0.0001$). The likelihood of a graft failure (including death) within one year for the low-volume surgeon group was 3.1 times higher than for the high-volume surgeon group ($p < 0.0001$); the trend was similar for hospital volume. Female patients had a lower risk than did male patients, and patients ≥ 55 years old and those with a higher Charlson comorbidity index score, had a higher risk of severe sepsis.

Conclusions: We conclude that the risk of severe sepsis and graft failure (including death) is higher for patients treated in hospitals and by surgeons with a low volume of renal transplantations. Therefore, the health authorities should consider exporting best practices through educational outreach and regulation and then providing transparent information for public best interest.

Key words: graft failure, population-based, renal transplantation, sepsis, volume-outcome relationship.

Introduction

Studies on surgeons and hospitals with higher caseloads provide evidence of better outcomes in major surgery, especially in cancer [1-3]; however, the association is controversial in different healthcare systems [4] and some types of surgery. Despite the benefits of volume, the controversy claimed it is due to the concentration of hospital care supply and also concerned medical skills loss in lower level hospital and patients will flow to higher level hospital.

Graft rejection and infection were the two major causes of death in renal transplant recipients from the 1970s until the mid-1980s [5]. Because of improved immunosuppressive protocols and surgical techniques, the incidence of graft rejection has impressively decreased [6]. Despite recent advances in management and therapy, postoperative infection remains high, around 40% [7-9], and exceeds acute rejection as the leading cause of hospitalization in renal transplant recipients with a functioning allograft [10]. Sepsis is a systemic and deleterious host response to infection, and severe sepsis is defined as sepsis with acute organ dysfunction, hypoperfusion (including oliguria, lactic acidosis, or encephalopathy), or hypotension [11, 12]. The incidence of severe sepsis after most elective operative procedures increased from 0.3% in 1997 to 0.9% in 2006 [13]. In the U.S., organ transplant recipients are at an especially high risk for developing severe sepsis [14]. It is the most common life-threatening complication of long-term immunosuppressive therapy and is the main reason for intensive care unit (ICU) admission of renal transplant recipients [8]. An ICU admission is associated with a decreased graft longevity rate and a higher post-transplantation mortality rate [8, 15]. Moreover, patients with severe sepsis might develop multiple septic episodes during the same hospitalization or after discharge [16, 17].

Multiple factors are associated with the development of severe sepsis after kidney transplantation, e.g., the intensity of exposure to potential pathogens (epidemiologic exposure) and the combined effect of all of the factors that contribute to a patient's susceptibility to infection [18]. Moreover, many factors contribute to the development of severe sepsis [18]. Preventing and managing severe sepsis places extraordinary demands, not only on surgeons, but also on other medical personnel, including anesthesiologists, diagnostic and interventional radiologists, critical care specialists, nursing, and nutritional support service workers.

The level of the surgeons' transplantation experience and the level of the hospital transplantation teams' quality of care may significantly contribute to reducing the incidence of severe sepsis

post-transplantation. Multiple studies [7, 19, 20] have shown an association between hospital volume and surgical outcomes for organ transplantations. However, the effect of surgeon or hospital volume on severe sepsis is not yet clear despite its being a key factor associated with both graft longevity and patient survival. This study aims to explore the relationship between the surgeon or hospital volume with consideration of the postoperative severe sepsis or graft-failure (including death). Therefore, we investigated this question on a nationwide scale using claims data from the Taiwan National Health Insurance Database.

Study population and Methods

Database

The data for this study were obtained from Taiwan National Health Insurance Research Database (NHIRD) of the Taiwan National Health Research Institute. The NHIRD, which covers nearly all inpatient and outpatient medical benefit claims for the Taiwanese population of over 22 million (about 99% of Taiwan's population in 2008), is one of the most comprehensive nationwide population-based data sources currently available and has been used extensively in many epidemiological studies. The NHIRD provides encrypted patient identification numbers, gender, date of birth, dates of admission and discharge, the ICD-9-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) codes of diagnoses (up to five) and procedures (up to five), details of prescriptions, and expenditure amounts. It also includes a registry of contracted medical facilities, and a registry of board-certified surgeons. With ethical approval from National Health Research Institute, we used data for the ambulatory care claims, all inpatient claims, and registry for patients with catastrophic illnesses for this study. All NHI datasets can be interlinked with each individual personal identification number.

Selection of patients and variables

All patients with end-stage renal disease (ESRD) who underwent kidney transplantation between January 1, 1999, and December 31, 2007, were identified by the ICD-9 CM procedure code 55.69. Patients with unknown gender or missing data were excluded. All patients were followed-up through December 31, 2008. Seventeen hundred seventy-nine kidney transplantations were done by 142 surgeons in 35 hospitals during this period.

Physicians and hospitals were categorized by their total patient volume by using their unique identifiers in the database. The sample of 1779 patients was divided into two groups: the low-volume group

(first 1/3) and the medium- and high-volume group (second 1/3 [medium-volume] and third 1/3 [high-volume]), based on physician volume: ≤ 33 transplantations (low-volume), and > 33 transplantations (medium- and high-volume), and the hospital sample was divided into two groups: ≤ 95 transplantations (low-volume), and > 95 transplantations (medium- and high-volume).

The two primary outcomes were severe sepsis and graft failure (including death). The ICD-9-CM codes for the sepsis in this study used the definition from Angus et al [21], severe sepsis was defined as sepsis complicated by organ dysfunction. The key independent variables were the kidney transplantation volumes both for physicians and for hospitals. Other physician attributes included age (≤ 40 , 40-49, and ≥ 50) and gender. The hospitals were grouped by public or private ownership. Patient characteristics included age (≤ 20 , 21-55, and > 55), gender, and modified Charlson Comorbidity Index score [22], which was used to infer the health status of each patient; higher sums of weighted scores indicated higher disease severity.

Statistical Analysis

Descriptive statistical analyses using Pearson χ^2 tests were done to compare the characteristics of patients, physicians, and hospitals with physician volume and hospital volume. The association between medical costs and physician volume, medical costs and hospital volume, length of stay in hospital and physician volume, and length of stay in hospital and hospital volume were determined using Student's t-test. Unconditional logistic regression analyses were used to assess the crude odds ratio of (1) severe sepsis and (2) graft failure (including death) at one year between the physician volume and hospital volume groups. Moreover, multivariate logistic regression using the generalized estimated equation method (GEE), which clusters hospital volume, was used to obtain the adjusted odds ratio (AOR) of graft failure (including death) at one year between the physician volume groups. GEE method accounts for the fact that patients within the same hospital volume group may be more similar to each other than they are to patients in other hospital volume groups because of specific physician and treatment practices.

Kaplan-Meier analysis was used to calculate the cumulative survival rates of graft failure (including death) after kidney transplantation in a 10-year (1999-2008) follow-up period, and the log-rank test was used to test the differences between the survival curves. Survival time was measured from the date of kidney transplantation until the day of graft failure or death or until the end of the study. SAS 9.3.1 (SAS

Institute, Cary, NC) was used for all statistical analyses. The alpha value indicated significance at the 0.05 level.

Results

The mean medical cost and length of stay (hospitalization) was significantly less in the high physician-volume groups than in the low physician-volume groups (new Taiwan dollars (NT\$) 195,223 vs. NT\$257,495; 17.56 vs. 19.84 days, respectively; $P < 0.0001$). There was no significant difference in the gender of the patients, but significantly ($P < 0.0001$) more than 80% of the patients were in the 21-55 years old age group in both the high- and low-volume groups. Interestingly, in the low-volume group, a higher proportion of patients had more comorbidities (CCI > 2). In addition, physician attributes (gender and age), were both significantly different ($P < 0.0001$) between the high- and low-volume physicians (Table 1).

The distributions of patient attributes were similar when stratifying by hospital volume. Mean medical cost was significantly lower in the high-volume hospital groups than in the low-volume hospital groups (NT\$205,784 vs. NT\$238,175, respectively; $P < 0.0001$), but mean length of stay was not significantly different (Table 2).

Table 1. The distributions of basic characteristics by physician volume with medical cost and length of stay.

	Physician Volume		P-value
	Low (1-33)	High (> 33)	
Total number of physicians	128	14	
Total number of patients	619 (34.79)	1160 (65.21)	
Mean medical cost (NT\$)	257,495 \pm 204,344	195,223 \pm 126,356	< 0.0001
Mean length of stay (days)	19.84 \pm 19.64	17.56 \pm 10.04	0.0013
Patient attributes			
Gender			
Male	308 (49.76)	557 (48.02)	
Female	311 (50.24)	603 (51.98)	0.4842
Age (years)			
≤ 20	46 (7.43)	57 (4.91)	0.0411
21-55	519 (83.84)	976 (84.14)	
> 55	54 (8.72)	127 (10.95)	
CCI score			
0	380 (61.39)	819 (70.61)	0.0002
1	157 (25.36)	239 (20.60)	
> 2	82 (13.25)	102 (8.79)	
Physician attributes			
Gender			
Male	593 (95.80)	1160 (100.00)	< 0.0001
Female	26 (4.20)	0	
Age (years)			
≤ 40	206 (33.28)	326 (28.10)	0.0003
40-49	281 (45.40)	486 (41.90)	
≥ 50	132 (21.32)	348 (30.00)	

NT\$, new Taiwan dollars; CCI, Charlson Comorbidity Index.

Table 2. The distributions of basic characteristics by hospital volume with medical cost and length of stay.

	Hospital Volume		P-value
	Low (≤ 95)	High (> 95)	
Total number of hospitals	30	5	
Total number of patients	610 (34.29)	1169 (65.71)	
Mean medical cost (NT\$)	238,175 ± 162,801	205,784 ± 158,420	< 0.0001
Mean length of stay(days)	18.58 ± 13.80	18.23 ± 14.35	0.626
Patient attributes			
Gender			
Male	307 (50.33)	611 (52.27)	0.2986
Female	303 (49.67)	558 (47.73)	
Age (years)			
≤ 20	26 (4.26)	77 (6.59)	0.0561
21-55	529 (86.72)	966 (82.63)	
> 55	55 (9.02)	126 (10.78)	
CCI score			
0	394 (64.59)	805 (68.86)	0.1816
1	149 (24.43)	247 (21.13)	
> 2	67 (10.98)	117 (10.01)	
Hospital attributes			
Hospital ownership			
Public	57 (9.34)	937 (80.15)	< 0.0001
Private	553 (90.66)	232 (19.85)	

NT\$, new Taiwan dollars; CCI, Charlson Comorbidity Index.

Table 3. One-year severe-sepsis rate with odds ratio across physician and hospital caseload-volume groups.

Risk Factor	None	Severe Sepsis	Odds Ratio (95% CI)	P-value
Severe sepsis in hospital				
Physician volume				
Low	568 (91.76)	51 (8.24)	1.65 (1.12-2.42)	0.0115
High	1100 (94.83)	60 (5.17)	1.00	
Hospital volume				
Low	550 (90.16)	60 (9.84)	2.39 (1.62-3.52)	< 0.0001
High	1118 (95.64)	51 (4.36)	1.00	
Severe sepsis within one year				
Physician volume				
Low	542 (87.56)	77 (12.44)	1.61 (1.17-2.22)	0.0033
High	1066 (91.90)	94 (8.10)	1.00	
Hospital volume				
Low	525 (86.07)	85 (13.93)	2.04 (1.48-2.80)	< 0.0001
High	1083 (92.64)	86 (7.36)	1.00	

CI, confidence interval.

Table 4. One-year graft-failure (including death) rate with odds ratios across physician and hospital caseload-volume groups

	None	Death	Odds Ratio	P-value
Death or graft failure within one year				
Physician Volume				
Low	584 (94.35)	35 (5.65)	3.10 (1.80-5.33)	< 0.0001
High	1138 (98.10)	22 (1.90)	1.00	
Hospital Volume				
Low	575 (94.26)	35 (5.74)	3.17 (1.85-5.46)	< 0.0001
High	1147 (98.12)	22 (1.88)	1.00	

Of the patients with a kidney transplantation who developed severe sepsis, about 8.24% were in the low-volume (OR: 1.65; 95% CI: 1.12-2.42; P = 0.0115) physician group versus about 5.17% in the

high-volume physician group (Table 3). Moreover, about 9.84% were in the low-volume hospital group (OR: 2.39; 95% CI: 1.62-3.52; P = 0.0001) versus about 4.36% in the high-volume hospital group. These findings remained significant even when we estimated the risk of developing severe sepsis within one year. The likelihood of death or graft failure within one year in the physician low-volume group was 3.1 times higher than in the high-volume group (95% CI: 1.80-5.33; P < 0.0001) and 3.17 times higher in the hospital low-volume (95% CI: 1.85-5.46; P < 0.0001) (Table 4).

We also analyzed 10-year patient survival using a log-rank test to compare the likelihood of graft failure (including death) based on physician-volume and hospital-volume (Figures 1, 2). The low-volume groups had a significantly (P < 0.001) higher risk in both instances.

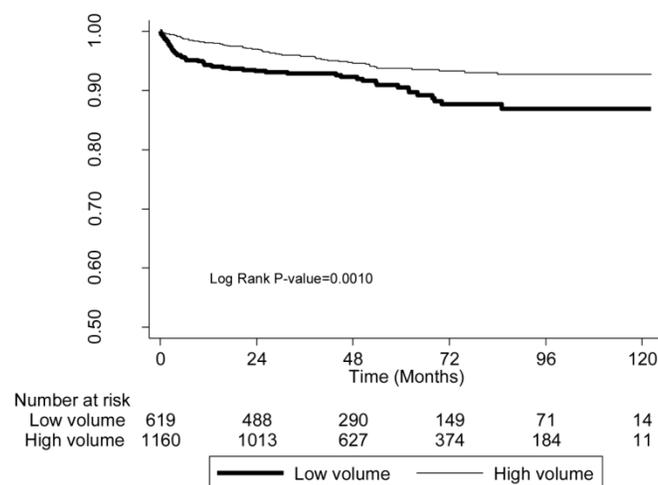


Figure 1. The survival curves of patients with kidneys transplanted by low-volume and high-volume physicians.

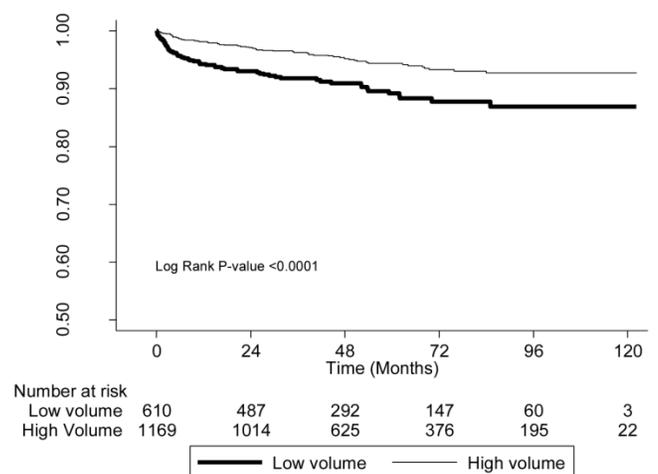


Figure 2. The survival curves of patients with kidneys transplanted in low-volume and high-volume hospitals.

To account for the possibility that patients within the same hospital-volume group may be more similar to each other than to patients in other hospital-volume groups because of specific physician and hospital treatment practices, we used a logistic regression model with the GEE method to explore the association of the 1-year severe sepsis risk with the same risk factors used for the other analyses. Patients treated by low-volume physicians still had 1.35 times the risk of developing severe sepsis than did patients treated by high-volume physicians. Physician gender was not a significant factor, but physician age was: patients treated by physicians ≤ 40 had a significantly lower risk (AOR: 0.633; $P < 0.0001$), but those treated by physicians > 50 had a significantly higher risk (AOR: 1.4; $P < 0.0022$). Female patients were significantly less likely to develop severe sepsis (AOR: 0.768; 95% CI: 0.619-0.953; $P < 0.0001$), but patients > 55 years old were significantly ($P < 0.0001$) more likely to develop it, as were patients with a higher CCI score (Table 5). Finally, patients treated in a private hospital were significantly ($P < 0.0001$) more likely to develop severe sepsis than were patients treated in a public hospital.

Table 5. Risk factors for one-year severe sepsis of kidney transplantation patients.

Risk Factor	Adjusted Odds Ratio (95% CI)	P-value
Physician attributes		
Physician volume	1.349 (1.254-1.452)	< 0.0001
Low		
High		
Gender		
Male		
Female	1.358 (0.449-4.109)	0.5881
Age (years)		
≤ 40	0.633 (0.616-0.651)	< 0.0001
40-49	Reference	
≥ 50	1.400 (1.129-1.737)	0.0022
Patient attributes		
Gender		
Male		
Female	0.768 (0.619-0.953)	0.0165
Age (years)		
≤ 20	1.241 (0.713-2.160)	0.4442
21-55	Reference	
> 55	1.411 (1.335-1.492)	< 0.0001
CCI Score		
0		
1	1.314 (1.216-1.421)	< 0.0001
> 2	1.583 (1.392-1.800)	< 0.0001
Hospital attributes		
Hospital ownership		
Public		
Private	2.537 (2.402-2.679)	< 0.0001

CCI, Charlson Comorbidity Index.

Discussion

In this study, we explored the relationship between physician and hospital volumes of kidney transplantations with postoperative severe sepsis and graft failure (including death). Several studies have reported serious postoperative complications because of sepsis, which is associated with a higher risk of mortality. We found that patient who had their transplantation surgery done either by high-volume physicians or in high-volume hospitals, had a lower risk of developing severe sepsis in the hospital, even within one year. Moreover, the risk of graft failure (including death) was significantly lower in the short term (within one year) and in the long term (~ 10 years) after a kidney transplantation in a high-volume hospital.

Since the first published article in English on the volume-outcome relationship [23], there have been numerous studies that provide similar results for research on, e.g., cardiovascular or orthopedic procedures and cancer surgery. High-volume hospitals not only have better survival rates, but they also have a lower infectious complication and reduced resource utilization [24, 25]. Scare studies in the kidney transplantation applied in the above two hypothesis (practice-makes-perfect or selective-referral), not only because the rare cases in kidney transplantation, but also the serious outcomes applied in a short time which produce the unstable predication.

The likelihood of graft failure (including death) within a year of the transplantation is significantly associated with each patient's personal characteristics, such as gender and age, and with relevant postoperative medical conditions, such as sepsis, which is consistent with other studies [26, 27]. We found that physician-volume was, indeed, related to the risk of severe sepsis, especially for the low-volume group, and recommend that health authorities consider certifying some institutions for economic reasons or to provide the transparent information about patient's choices of hospital for quality-procedures-and-outcomes reasons.

Patient characteristics, operative time, and the identity of the surgeon are perhaps the three most important factors the affect surgery outcomes [28]. Although one study found a significant volume-outcome relationship at the physician level but not at the hospital level [29], there remain many unexplained factors to analyze before the relationship can be confirmed. One study [30] claims that a physician's skill or experience is important for determining clinical outcomes; however, other studies [31, 32] conclude that the volume of procedures is not the sole determiner of better outcomes and are concerned that physician overload may also affect the quality. If

volume significantly affects outcomes, national departments of health may want to encourage the centralization of procedures in a few facilities. In addition, hospitals may have the benefit of producing better outcomes when treating only one or a few conditions [33]. Otherwise, healthcare officials may consider requiring surgeons to take additional training and education in the low-volume procedures that they perform, or enforcing the referral system for low-volume hospitals and implement some useful quality-improvement strategies for patients.

Based on all these findings, we may be able to infer some key economic implications for the feasibility and likelihood of volume-related policy options in some disease areas [34]. In addition, patients with chronic kidney disease (CKD) benefits from National Health Insurance (NHI) can apply for a catastrophic illness certificate, which grants exemption from all copayments to reduce most financial barriers for treatment under the universal healthcare system in Taiwan. For patients with CKD in Taiwan, the barriers of accessibility or finance were considerably lower than in other countries to encourage them to undergo treatment. However, even though we may find a positive relationship between outcomes and volume, it is difficult to reach consensus on a cut-point for "low volume". Health authorities may want to consider improving the efficiency of their national referral systems to increase the quality of care and reduce mortality in their countries' hospitals [35].

This study has several limitations. First, the shortage of evidence supporting the hypothesis is that the volume-outcome association involves a causal relationship. For transplantation, an inverse volume-outcome relationship appears to exist [20, 36], but studies still need to consider several influences, such as patient and donor selection, case mix, timeliness of donor availability, operative technique, and so on. Moreover, one study [37] found comparable 90-day, 1-year, and 3-year survival outcomes between patients with end-stage renal disease (n = 14) and hepatocellular carcinoma (n = 14) who had undergone liver transplantation at a low-volume hospital. In addition, the NHI claim databases did not provide information related to kidney disease (for example, National Quality Forum measurement). Therefore, we are always to be cautious in the volume-outcome relationship.

Conclusions

Numerous studies have reported a positive association between high-volume physicians and better outcomes, but the debate for the threshold of a composite patient safety score for U.S. hospitals, which the Leapfrog Group has established [38], has still not

ended; or perhaps the existing findings encourage patients to prefer facilities with better-than-expected outcomes and away from those with worse-than-expected outcomes. Moreover, despite studies [39] that have confirmed the volume-outcome relationship, more appropriate statistical tools are suggested to clarify some unsatisfactory situations. The findings also imply that training and staffing levels are important factors. Therefore, defining and exporting best practices through education outreach, and, if necessary, government regulation must be part of the national health policy agenda.

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Competing interests

The authors declare that they have no competing interests.

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